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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/914,332	07/15/1997	SCOTT W. VAN ARSDELL	04599/005001	8315

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EXAMINER

RAMIREZ, DELIA M

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/13/2002

33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/914,332

Applicant(s)

VAN ARSDELL ET AL.

Examiner

Delia M. Ramirez

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 23-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 July 1997 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Art Unit: 1652

DETAILED ACTION

Status of the Application

Claims 1-31 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicants elected without traverse Group I, claims 1-22 in Paper No. 10, filed on 11/19/1998. Claims 23-31 are withdrawn from consideration as being drawn to a non-elected invention.

The request filed on 1/2/2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/914332 is acceptable and a CPA has been established. An action on the CPA follows.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The specification is objected to for the following reasons. While the specification discloses that a biological deposit has been made and that such deposit will be available to the public, no disclosure of the name and address of the depository has been provided. See 37 CFR 1.809(d). Correction is required.

Art Unit: 1652

Drawings

2. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review. Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application. In addition, if amendments to the specification are needed due to drawing corrections, Applicant is requested to submit such amendments while the case is being prosecuted to expedite the processing of the application.

Claim Objections

3. Claims 1-4, 11, 13, 21 are objected to because of the recitation of "DAPA", "SAM", or "bioA". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1652

6. Claims 1, 6, 17 and 18 (claims 3, 7-16, 18-22 dependent thereon) are indefinite in the recitation of "precursor is exogenously added to the culture and totals at least 10 mmoles per liter" as it is unclear what totals 10 mmoles per liter. It is suggested that if the term "totals at least 10 mmoles per liter" refers to the concentration of precursor in the culture, the claim be amended with more clear and unambiguous language, such as "precursor is exogenously added to the culture at a concentration of 10 mmoles per liter" or similar. For examination purposes, the claim will be interpreted as being drawn to a method wherein the concentration of the precursor in the culture is 10 mmoles per liter (10 mM). Correction is required.

7. Claims 2, 11, 21 (claims 4-10, 12-20 and 22 dependent thereon) are indefinite in the recitation of "bacterium is deregulated with respect to lysine production" or "bacterium is deregulated with respect to at least one biotin synthetic pathway" as it is unclear what the meaning of the term "deregulated" is as it relates to a bacterium. If the intended meaning of the term is a bacterium wherein lysine production is not regulated or bacterium wherein the biotin synthetic pathway is not regulated, the claims should be amended to recite "bacterium wherein lysine production is deregulated", "bacterium wherein the biotin synthetic pathway is deregulated" or similar. For examination purposes, the claims will be interpreted as being directed to a method which uses a bacterium wherein lysine production or the biotin synthetic pathway is deregulated. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1652

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. Claims 1 and 3 are directed to a method of producing biotin vitamers which uses a genus of bacteria comprising a genus of lysine-utilizing diaminopelargonic acid (DAPA) aminotransferases, claims 2, 4-12 are directed to the method as described above wherein the lysine production or any biotin synthetic pathway in the bacteria is deregulated in any way, and claims 13-22 further add the limitation that the method uses a genus of bacteria comprising a genus of lysine-utilizing DAPA amino transferases and a genus of S-adenosylmethionine (SAM)-utilizing DAPA transferases. While the specification discloses *B. subtilis* or *E. coli* wherein the gene encoding DAPA aminotransferases (*bioA*) from *B. subtilis*, *E. coli* or *S. marcescens* is expressed, no disclosure of the structure of other lysine or SAM-utilizing DAPA aminotransferases from other organisms as encompassed by the claims, is provided. While the specification mentions which enzymes can be mutated to deregulate lysine or biotin synthesis and specifically discloses 4 enzymes (aspartokinase I, II, III and DAP decarboxylase) in *B. subtilis* wherein modifications to the corresponding genes result in deregulation of lysine biosynthesis (Table 7), no disclosure of the structure of the enzymes or the specific mutations which can inactivate enzymes involved in the regulation of lysine production or biotin synthesis in other microorganisms, as encompassed by the claims, has been provided. Other methods which would lead to deregulation of lysine or biotin synthesis such as the addition of chemicals,

Art Unit: 1652

have not been described either. There is no disclosure of the critical structural elements required to display lysine or SAM-utilizing DAPA aminotransferase activity or which are the critical structural elements required to display aspartokinase I, II, III or DAP decarboxylase activity.

11. While one can argue that the structure of enzymes of similar function can be obtained by sequence comparison with a known protein of known function, the state of the art teaches that sequence comparison alone should not be used to determine a protein's function and that small amino acid changes can drastically change the function of a polypeptide. Bork (Genome Research, 10:348-400, 2000) teaches protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. The specification discloses only a few species of the genera of microorganisms, lysine and SAM-utilizing DAPA aminotransferases, enzymes involved in the regulation of lysine and biotin synthesis and mutations to said enzymes, to practice a method for producing biotin vitamers which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed method. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

Art Unit: 1652

12. Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of biotin vitamers using *E. coli* or *Bacillus subtilis* wherein said microorganisms express *E. coli*, *B. subtilis* or *S. marcescens* DAPA aminotransferases and wherein the lysine or biotin synthesis in *E. coli* or *B. subtilis* is deregulated by mutations in the genes encoding aspartokinase I, II, III or DAP decarboxylase, does not reasonably provide enablement for practicing the claimed method using any microorganism capable of expressing any lysine and/or SAM-utilizing aminotransferase wherein lysine or biotin synthesis is deregulated in any way. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

13. The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

14. Claims 1 and 3 are directed to a method of producing biotin vitamers using any bacteria capable of expressing any lysine-utilizing diaminopelargonic acid (DAPA) aminotransferase, claims 2, 4-12 are directed to the same method provided that lysine or biotin synthesis be deregulated in any way in said bacteria, and claims 13-22 further add the limitation that the method uses any bacteria capable of expressing any lysine-utilizing and any SAM-utilizing DAPA aminotransferases. The specification discloses *B. subtilis* or *E. coli* wherein the gene encoding DAPA aminotransferases (*bioA*) from *B. subtilis*, *E. coli* or *S. marcescens* is

Art Unit: 1652

expressed. In addition, the specification discloses the deregulation of the lysine biosynthetic pathway by mutations in 4 enzymes in *B. subtilis* (Table 7) and mentions which enzymes can be inactivated in the biotin biosynthetic pathway which would lead to deregulation of biotin synthesis. However, the specification fails to provide the structure of other lysine or SAM-utilizing DAPA aminotransferases, the structure or function of other enzymes involved in the regulation of lysine or biotin synthesis and the specific modifications in the corresponding genes which would deregulate the synthesis of lysine or biotin, or other methods, such as the addition of chemicals, which would also deregulate the synthesis of lysine or biotin.

15. As indicated above, the state of the art is unpredictable with regard to isolating proteins of similar function based on sequence homology. See the teachings of Bork (Genome Research, 10:348-400, 2000), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), and Broun et al. (Science 282:1315-1317, 1998) already discussed. Since the amino acid sequence of a protein determines its structural and functional properties, one of skill in the art would require some knowledge and guidance as to how structure is related to function in order to (1) isolate enzymes with similar function to those required by the claimed method, and (2) determine which amino acid modifications (substitutions, deletions, insertions) would inactivate a gene encoding an enzyme involved in the regulation of lysine or biotin synthesis. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to maintain the desired function, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) screen and isolate those polypeptides, as encompassed by the claim, with lysine and/or SAM-utilizing DAPA

Art Unit: 1652

aminotransferase activity, (2) isolate those enzymes involved in lysine or biotin biosynthesis, (3) identify the modifications in such enzymes which would lead to deregulation of lysine or biotin biosynthesis, or (4) identify methods which would result in deregulation of lysine or biotin biosynthesis. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 1, 3, 7, 11-19, 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Bower et al. (EP-0-635-572-A2, published on January 25, 1995; cited in IDS Paper No. 5, filed on 2/20/1998).

Bower et al. teaches the *B. subtilis* strain BI282 which was made by integration of the plasmids pBIO168 and pBIO152 into the chromosome, allowing the insertion of the *bioA*, *bioF*, *bioD*, *bioB*, *bioI*, and *bioW* under the SP01-15 promoter (Table 7, last item; Figure 16). As a result, the BI282 strain is able to overproduce a lysine-utilizing DAPA aminotransferase (product of the *bioA* gene). Bower et al. also teaches the production of biotin vitamers and biotin (Table 10, last item, Table 12, last item) by cultivating BI282 in medium containing veal infusion broth

Art Unit: 1652

and yeast extract as the main sources of amino acids (Table 11, first two items) at concentrations of 33.3 (150/4.5) g/liter and 6.6 (30/4.5) g/liter, respectively.

Claims 1, 3 and 7 are drawn to a method of producing biotin vitamers, including biotin, with any bacterium capable of producing a lysine-utilizing DAPA aminotransferase wherein the bacterium is cultured in medium containing at least 10 mM of lysine or lysine precursors. Claim 11 adds the limitation that biotin synthesis in the bacterium be deregulated and claim 12 requires that the biotin vitamer be biotin in addition to the limitation of claim 11.

Since the *bioA* gene overexpressed in BI282 is from *B. subtilis*, the strain overproduces a lysine-utilizing DAPA aminotransferase. Also, since veal infusion broth and yeast extract are used, based on the typical concentrations of lysine in yeast extract (see DIFCO Manual), the media used comprise at least 10 mM lysine. Furthermore, biotin synthesis is deregulated in the BI282 strain since the genes for *bioF*, *bioD*, *bioB*, *bioI*, and *bioW* from *B. subtilis* are overexpressed, which result in higher levels of biotin vitamers produced (Table 10) compared to the wild-type strain. Therefore, the teachings of Bower et al. anticipate the claims as written.

Bower et al. also teaches the strain *E. coli* MM294 (wild-type for biotin biosynthetic genes), which comprises a plasmid (pBIO289) wherein said plasmid comprises the genes *bioA* (lysine-utilizing DAPA aminotransferase), *bioF*, *bioD*, *bioB*, *bioI* and *bioW* from *B. subtilis* (Examples V and VI). Bower et al. also teaches the production of biotin and biotin vitamers (Table 4) by cultivating said *E. coli* strain in rich medium (page 16, lines 17-20).

Claims 13-19 are directed to a method of producing biotin vitamers, including biotin, with any bacterium capable of producing a lysine-utilizing DAPA aminotransferase and a SAM-utilizing DAPA aminotransferase by culturing said bacterium in a medium which has at least 10

Art Unit: 1652

mmoles per liter of lysine or lysine precursors and any amount of methionine or SAM analogs.

Claim 21 adds the additional limitation that biotin synthesis be deregulated in the bacterium and

claim 22 requires that the biotin vitamer be biotin in addition to the limitation of claim 21.

Since the *E. coli* strain is wild type for biotin biosynthetic genes, this strain inherently contains a biotin gene encoding a SAM-utilizing DAPA aminotransferase (*E. coli* bioA) and therefore produces a SAM-utilizing DAPA aminotransferases. Similarly, since the plasmid contains the bioA gene from *B. subtilis*, the strain can also express a lysine-utilizing DAPA aminotransferase. Also, since rich medium, as known in the art, would have at least yeast extract and hydrolyzed protein (tryptone and/or casamino acids), at least 10 mM lysine or lysine precursor and methionine are present in the medium. Furthermore, biotin synthesis is deregulated in the *E. coli* strain of Bower et al. since the genes for bioF, bioD, bioB, bioI, and bioW from *B. subtilis* are overexpressed in the *E. coli* host cell, which result in higher levels of biotin vitamers produced (Table 4) compared to the wild-type strain. Therefore, the teachings of Bower et al. anticipate the claims as written.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

18. Claims 1, 3, 7, 11-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Bower et al. (US Patent No. 6057136, filed on July 8, 1996).

Art Unit: 1652

19. This rejection was applied to claims 1, 3, 7, 11-22 by the previous Examiner of record and is discussed in Paper No. 28.

20. Applicants argue that each and every element recited in the claim should be taught by the prior art reference and that these elements should be arranged as in the claim, therefore the "expectation" of the media taught by Bower et al. having at least 10 mmoles per liter of lysine, lysine precursor or methionine is not sufficient evidence to show that the reference teaches that limitation. Similarly, applicants argue that there is no factual or technical evidence to support the inherency argument that the aminotransferase of the strain BI282 taught by Bower et al. is in fact a lysine-utilizing DAPA aminotransferase. Furthermore, Applicants assert that even if the media taught by Bower et al. contains methionine or at least 10 mmoles per liter of lysine or lysine precursor, the reference does not teach literally or inherently the step of "exogenously adding" lysine, lysine precursor or methionine.

21. Applicants arguments have been fully considered but are not deemed persuasive to overcome the rejection. Although the reference does not specifically teach that the media contains methionine or at least 10 mmoles per liter of lysine or lysine precursor, as indicated above, it is well known in the art that yeast extract alone will provide amino acids, peptides, and vitamins because yeast extract is the water soluble portion of autolyzed yeast. Typical concentrations of methionine and lysine for such extracts are shown in the DIFCO Manual. As such, the limitations of the claims are clearly present in the methods of Bower et al. Since the office does not have a laboratory to test the media taught by the reference, it is applicant's burden to show that the media of Bower et al. does not contain lysine, lysine precursor, or methionine in the quantities recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA

Art Unit: 1652

1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). In regard to the step of "exogenously adding" the amino acids lysine, methionine or the lysine precursor, it is not clear how the term "exogenously adding" could be any different from "adding" media components (yeast extract and veal infusion broth) which would also have lysine, methionine, or lysine precursors.

22. In regard to the arguments that the strain BI282 taught by Bower et al. does not have a lysine-utilizing DAPA aminotransferase, while it is agreed that the reference does not specifically teach that the *B. subtilis* bioA gene product (DAPA aminotransferase) is a lysine-utilizing aminotransferase, such property (lysine utilization) is inherently present since the specification discloses that the *B. subtilis* bioA gene product (DAPA aminotransferase) is a lysine-utilizing DAPA aminotransferase (page 10, lines 24-27). Therefore, the property disclosed by Applicants in regard to lysine utilization of Applicant's DAPA aminotransferase would also apply to the DAPA aminotransferase of Bower et al. since both DAPA aminotransferases are the same (from *B. subtilis*).

23. It is noted that due to a typographical error, claim 20 was rejected under 102(e) by the previous Examiner of record. This rejection as it applies to claim 20 is hereby withdrawn.

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

25. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

26. Claims 8 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bower et al. (EP 0-635-572-A2, January 25, 1995; cited in IDS Paper No. 5, filed on 2/20/1998) in view of Yamada et al. (US Patent No. 4563426, January 7, 1986; cited in previous Office Action Paper No. 28). The teachings of Bower et al. have been discussed above. Bower et al. does not teach the conversion of dethiobiotin produced by bacteria into biotin by a separate fermentation. Yamada et al. teaches the conversion of dethiobiotin into biotin by a fermentation process (columns 3-4, Example 2). Yamada et al. does not teach dethiobiotin production by recombinant *B. subtilis* or *E. coli*.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to convert dethiobiotin into biotin through a fermentation process, as taught by Yamada et al., with dethiobiotin made by bacteria, as taught by Bower et al. A person of ordinary skill in the art is motivated to convert dethiobiotin into biotin using a fermentation process because biotin is an essential vitamin for all organisms, therefore any process which can produce this vitamin in large amounts is highly desirable. One of ordinary skill in the art has a reasonable expectation of success at making biotin from dethiobiotin using a fermentation

Art Unit: 1652

process since Yamada et al. teaches the conversion of dethiobiotin into biotin through a fermentation process. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

27. Claims 8 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bower et al. (US Patent No. 6057136; cited in previous Office Action Paper No. 28) in view of Yamada et al. (US Patent No. 4563426, January 7, 1986; cited in previous Office Action Paper No. 28).

28. Applicant has provided evidence showing that the invention was owned by, or subject to an obligation of assignment to, the same entity as US Patent No. 6057136 at the time this invention was made. Accordingly, Bower et al. (US Patent No. 6057136) is disqualified as prior art through 35 U.S.C. 102(e), (f) or (g) in any rejection under 35 U.S.C. 103(a) in this application. This rejection is hereby withdrawn

Conclusion

29. No claim is in condition for allowance.

30. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

31. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE

Art Unit: 1652

COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

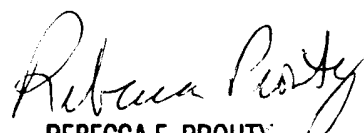
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288.

The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
August 8, 2002


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1800
1652